REMARKS

Reconsideration of the rejections set forth in the Office Action dated January 8, 2008 is respectfully requested in view of the foregoing amendments and following remarks.

I. Claim Amendments

Claim 1 has been amended to clarify the claimed subject matter with respect to the interferon-tau dosage. Support for the amendment can be found in the specification at, *e.g.*, ¶¶ [0073], [0079], [0084], [0104], and [0126].

No new matter has been added.

II. Rejection under 35 U.S.C. § 112, first paragraph (enablement)

Claims 1, 2, 4-6, 14, and 15 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. Specifically, the Examiner asserted that the claims read on a large number of polypeptides that would not be capable of increasing the IL-10/IFN-γ ratio.

The rejection is traversed in view of the following arguments and foregoing amendment.

A. Legal Standard

The standard for establishing whether an application's disclosure satisfies the enablement requirement is whether one skilled in the art could practice the claimed invention without undue experimentation. An application need not teach and preferably omits that which is known in the art. M.P.E.P. at 2164.01.

B. Analysis

The rejected claims require the polypeptide to be "interferon tau" and require the polypeptide to "produce an initial measurable increase in the subject's blood IL-10 level, relative to the blood IL-10 level in the subject in the absence of interferon-tau administration, with (i) no substantial change in the subject's blood IFNγ level relative to

the IFNγ level in the absence of interferon-tau administration or (ii) a decrease in the subject's blood IFNγ level relative to the IFNγ level in the absence of interferon-tau administration." Therefore, the Examiner's assertion that the claim would read on polypeptides that would not be capable of increasing the IL-10/IFN-γ ratio, is technically incorrect in view of the claim language that *requires* the claimed polypeptides to increase the IL-10/IFN-γ ratio, or else be excluded from the claimed genera of interferon-tau polypeptides. The specification would enable the skilled artisan to use any of polypeptides that *do* meet the requirements of the claim language, to be used to increase the IL-10/IFNγ ratio in subjects suffering from multiple sclerosis. Enablement is a question of whether one skilled in the art could practice a *claimed invention* without undue experimentation, and, here, the claimed *method* can be practiced without undue experimentation using the polypeptides encompassed by the claim language.

The question of whether Applicants have adequately *described* the claimed polypeptides in the specification seems better characterized as a written description issue, which Applicants also address, immediately below.

Accordingly, withdrawal of the rejection is respectfully requested.

III. Rejection under 35 U.S.C. § 112, first paragraph (written description)

Claims 1, 2, 4-6, 14, and 15 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description for interferon-tau polypeptides.

A. Legal Standard

The standard for establishing whether an application's disclosure satisfies the written description is whether one skilled in the art can reasonably conclude that Applicant had possession of the claimed invention. What is conventional or well known to one of ordinary skill in the art need not be disclosed in detail. M.P.E.P. at 2163.

B. Analysis

The Patent Office's own Written Description Training Materials (published March 25, 2008; herein "March 2008 Training Materials") address claim language directed to sequence homology and function as they pertain to polypeptide variants (pp. 31-42).

Referring to Example 11 of the March 2008 Training Materials, Example 11B presents a first claim (claim 1) that refers to a polypeptide having homology to a SEQ ID NO (*i.e.*, "at least 85% amino acid sequence identity to SEQ ID NO: 2"), and a second claim (claim 2) that includes the same homology language in addition to functional language (*i.e.*, "activity Y").

In evaluating the compliance of this hypothetical claim 1 to the written description requirement, the Patent Office finds that "one of ordinary skill would be able to use conventional . . . techniques to routinely generate and identify nucleic acids that encode . . . any polypeptide having 85% structural identity to SEQ ID NO: 2." (*Id.* at 41.) Accordingly, claim 1 satisfies the written description standard.

Hypothetical claim 2 in Example 11B of the March 2008 Training Materials, which includes the same 85% sequence identity language and further includes functional language, also satisfies the written description requirement because "a correlation exists between the function of the claimed protein and the structure of the disclosed binding and catalytic domains." (*Id.*) The paragraph concludes, "[b]ased on applicant's disclosure and the knowledge within the art, those of ordinary skill in the art would conclude that the applicant would have been in possession of the claimed genus . . . " (*Id.*)[1] Example 11B of the March 2008 Training Materials was distinguished from Example 11A, which recited similar claim language; however, there was "no disclosed or art-recognized correlation between any structure other than SEQ ID NO: 2 and novelty activity X." (*Id.* at 38.)

In the present case, Applicants have disclosed structure-function information about interferon-tau (*e.g.*, ¶¶ [0038] and [0048-0051]), particularly relating to the first 172 amino acid residues. In addition, there is an *abundant* amount of structure-function information available in the art regarding interferon-tau, some of which is of record in the present case. Finally, the claimed level of sequence identity is "at least 90%,"

---

[1] That the exemplary claims referred to nucleic acids encoding particular polypeptides, rather than polypeptides, directly, would not appear to change the analysis, since the homology and functional language concerned the polypeptides, not the nucleic acid encoding the polypeptides.

which is less than the 85% identity that was used in Examples 11A and 11B of the March 2008 Training Materials.

Applicants submit that the present claim language clearly falls within the Patent Office's own guidelines for complying with the written description requirement under 35 U.S.C. § 112, first paragraph because - in view of the disclosure, what is known in the art, and the recited level of homology, one skilled in the art would recognize that Applicants has possession of the claimed subject matter.

Withdrawal of the written description rejection is respectfully requested. In the event that the rejection is maintained in a future Office Action, Applicants request that the Examiner clearly articulate how the pending claims differ in substance from those of Example 11B of the March 2008 Training Materials, referred to above and clearly articulate the applied standard.

III. Rejection under 35 U.S.C. § 103

Claims 1, 2, 4-6, 14, and 15 were rejected under 35 U.S.C. § 103(b) as allegedly obvious over Soos *et al.* (WO 97/33607) in view of van Boxel-Dezaire *et al.* ((1999) *Ann. Neurol.* 45:695-703). The rejection is respectfully traversed.

A. The Pending Claims

Independent claim 1, as amended, recites, "[a] method of increasing IL-10/IFNγ ratio in subjects suffering from multiple sclerosis, comprising orally administering interferon-tau to the subject at a daily dosage of greater than about 1×10^9 Units to produce an initial measurable increase in the subject's blood IL-10 level, relative to the blood IL-10 level in the subject in the absence of interferon-tau administration, with (i) no substantial change in the subject's blood IFNγ level relative to the IFNγ level in the absence of interferon-tau administration or (ii) a decrease in the subject's blood IFNγ level relative to the IFNγ level in the absence of interferon-tau administration, and continuing to orally administer interferon-tau to the subject on a regular basis of at least several times per week, independent of changes in the subject's blood IL-10 level, until a desired clinical endpoint is achieved, wherein the interferon-tau has at least 90% sequence homology to the polypeptide of SEQ ID NO: 2.

B. The Cited References

SOOS *ET AL.* (WO 97/33607) teach orally administering a therapeutically-effective amount of interferon-tau at a dosage of up to 1 x 10^8 Units/day, and preferably at a dosage of from 1 x 10^6 to 1 x 10^7 Units/day (page 5, lines 11-13; page 20, lines 2-4).

VAN BOXEL-DEZAIRE *ET AL.* describe the relationship between multiple sclerosis and IL-10 mRNA levels. The reference does not address interferon-tau.

C. Analysis

Among the considerations in determining whether a claim is obvious in view of a combination of cited references is whether the references teach each and every element of the claimed invention.

In the present case, none of the references, separately or in combination, teach orally administering interferon-tau to a subject at a daily dosage of greater than about 1 x 10^9 Units, as required by claim 1. Soos *et al.* teach that, in view of its lower toxicity, interferon-tau can be administered at higher doses than, *e.g.*, interferon-beta (page 20, lines 2-5), in particular a dose of up to 1 x 10^8 Units/day. The preferred range is 1 x 10^6 to 1 x 10^7 Units/day (*Id.*).

The presently claimed dosage of at least about 1 x 10^9 Units/day is about an order of magnitude greater than any dosage described by Soos *et al.*, and about two orders of magnitude greater than the preferred dosage range described by Soos *et al.* Soos *et al.* provide no motivation to use greater than 1 x 10^8 Units/day interferon-tau.

van Boxel-Dezaire *et al.* do not discuss interferon-tau, and does not cure the defect with respect Soos *et al.*

Since none of the references, separately or in combination, teach administering interferon-tau at a dosage of greater than about 1 x 10^9 Units/day, Applicants submit that the present claims are nonobvious in view of the reference. Withdrawal of the rejection is respectfully requested.

IV. Conclusion

Applicants believe that the present application is fully in condition for allowance. Early notice to this effect is earnestly requested. If the Examiner has any questions or

believes a telephone conference would expedite prosecution of this application, the Examiner is encouraged to call the undersigned at (650) 838-4300.

Respectfully submitted,
Perkins Coie LLP

Date: May 12, 2008

/Stephen Todd/
Stephen Todd
Registration No. 47,139

Correspondence Address:
Customer No. 22918